REMARKS

Claims 1, 12, 13, 18, 19, 21, 23-25, 28-31, 33-36, and 38-50 are currently pending in this application. Claims 12, 13, 18, 19, 29-31, and 41-49 stand withdrawn. Claims 1, 25, 33, and 35 are currently amended. Claims 28 and 50 are cancelled without prejudice or disclaimer as to the subject matter thereof. Claims 2-11, 14-17, 20, 22, 26, 27, 32, and 37 were previously cancelled without prejudice or disclaimer as to the subject matter thereof. Applicants respectfully reserve the right to prosecute the subject matter of the cancelled claims in one or more Continuation or Divisional applications.

Claim Amendments

Applicants respectfully submit that no new matter is introduced into the application by way of the instant claim amendments. Support for the term "immunogenic composition" in claims 25 and 35 is found throughout the specification, including the following disclosures:

> Page 14, lines 24-26 of the specification, which states that "[a]s the peptides of the invention are relatively small molecules it may be required in such compositions to combine the peptides with various materials such as adjuvants, to produce vaccines, immunogenic compositions, etc." (emphasis added).
>
> Page 16, lines 1-4 of the specification, which states that "[i]n preferred embodiments, the pharmaceutical composition of the invention is an immunogenic composition or vaccine capable of eliciting an immune response to a cancer disease" and that "[a]s used herein, the expression 'immunogenic composition or vaccine' refers to a composition eliciting at least one type of immune response directed against cancer cells." (emphasis added)

Support for the amendment to claim 1 regarding a C_{50} value of at most 20 μM is found throughout the application as originally filed, *inter alia*, on page 5, lines 16-18. Accordingly,

Applicants submit that no new matter is introduced into the application by way of the instant claim amendments.

Rejections

35 U.S.C. § 112, 1st Paragraph, Written Description

Claims 1, 21, 23-25, 28, 33-36, 38-40 and 50 were rejected under 35 U.S.C. § 112, 1st paragraph as allegedly failing to comply with the written description requirement.

The Office Action states (in part) that "[t]he specification does not disclose a representative number of species of MHC Class I-restricted epitope peptides as claimed ... the claims encompass a peptide that may comprise SEQ ID NO:5 or a subsequence of SEQ ID NO:5 with undisclosed flanking sequences not necessarily from the protein of origin, or composition, vaccine or complex thereof. The claims encompass a peptide that may be any MHC Class I-restricted epitope peptide, not just HLA-A2.1 that binds SEQ ID NO:5" *See* Office Action, page 3, lines 15-21. The Office Action further asserts that the specification lacks a representative number of species to support the scope of the claims.

Applicants respectfully disagree and traverse this rejection.

Applicants note that claim 1 has been amended to recite that the epitope peptide has a C_{50} value, defined as the concentration of the peptide required for half-maximal binding to HLA-A2, which is at the most 20 μM. Dependent claim 21, reciting a peptide capable of eliciting INF-g-producing cells in a PBL population of a cancer patient at a frequency of at least 10 per 10^4 PBLs, remains pending.

Applicants note that the Office Action interprets the claim for examination purposes to include peptides incorporating a subsequence of SEQ ID NO:5 with undisclosed flanking sequences not necessarily from the protein of origin. Following this interpretation presented in the Office Action, Applicants submit that a reasonably representative number of epitope peptides meeting the elements of claim 1 are set forth in the specification. For example, the specification contemplates the epitope peptides Sur9 (SEQ ID NO:3) and Sur1L2 (SEQ ID NO:4), which each

comprise a subsequence of SEQ ID NO:5 (namely "LGEFLKL"). *See* specification, page 23, Table 1. Furthermore, all three of these epitope-derived peptides have C_{50} (μM) values of at most 20 μM. *Id.*

It is also noted that in Example 2 of the specification the reactivity of these three epitope-derived peptides was measured in peripheral blood lymphocytes (PBLs) by ELISPOT from ten HLA-A2 positive breast cancer patients, fourteen HLA-A2 positive melanoma patients, and six chronic lymphatic leukemia (CLL) patients. According to the specification, "[t]he ELISPOT assay was used to quantify peptide epitope-specific IFN-γ releasing effector cells and has been described previously ..." *See* specification, page 27, lines 30-31.

The results demonstrate that at least several patients, represented by each category of cancer, responded to each of the respective epitope-derived peptides (Sur1, Sur9, Sur1M2) by eliciting IFN-γ producing cells at a frequency of at least 10 per 10^4 PBL. *See* specification, page 29, Table 2. Thus, Applicants submit that a reasonably representative number of epitope-derived peptides comprising SEQ ID NO:5 (as interpreted in the Office Action) satisfy the elements of dependent claim 21 as well.[1] Applicants submit that it is understood that patient-to-patient variability exists in the responses to the epitope-derived peptides encompassed by the pending claims. This is evidenced by the data presented in Table 2 and Figure 3, as well as the results of Examples 1 and 2. Nevertheless, Applicants submit that a reasonably representative number of epitope-derived peptides, in light of this patient-to-patient variability, is presented in the specification to support the scope of the amended claims.

In light of the instant amendments and remarks provided herein, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1, 21, 23-25, 33-36, and 38-40 under 35 U.S.C. § 112, 1st paragraph as allegedly failing to comply with the written description requirement. Applicants note that rejected claims 28 and 50 are cancelled herein without prejudice or disclaimer.

35 U.S.C. § 112, 1st Paragraph, Enablement

- **Claims 1, 21, 23-25, 28, 33-36, 38-40 and 50**

Claims 1, 21, 23-25, 28, 33-36, 38-40 and 50 were rejected under 35 U.S.C. § 112, 1st paragraph as allegedly failing to comply with the enablement requirement.

The Office Action states that the claims encompass an MHC Class I-restricted epitope peptide that comprises either SEQ ID NO:5 or a subsequence of SEQ ID NO:5 with undisclosed flanking sequences not necessarily from the protein of origin, and that the claims are larger than that of the exemplified Sur1M2 peptide. *See* Office Action, page 12. The Office Action asserts that the specification lacks a representative number of species to support the scope of the claims. The Office Action further asserts that the evidentiary references teach unpredictability in the art of predicting T cell epitope peptides (citing to Celis et al), and that the evidentiary references speak to unpredictability in the art in peptide vaccines or compositions and their inherent lack of immunogenicity in the art in peptide vaccines or compositions and their inherent lack of immunogenicity by themselves. The Office Action, while acknowledging that completed human clinical trials are not required to satisfy enablement, nevertheless again cites to a statement attributed to Dr. Anderson that phase III clinical trials are the only firm proof that a vaccine works. *See* Office Action, paragraph bridging pages 12-13.

Applicants respectfully disagree and traverse this rejection.

The Office Action Under 35 U.S.C. §112 ¶ 1, the "enablement requirement is satisfied when one skilled in the art, after reading the specification, could practice the claimed invention without undue experimentation."[2] "The fact that some experimentation is necessary does not

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[1] Claim 21 recites: A peptide according to claim 1 that is capable of eliciting INF-γ -producing cells in a PBL population of a cancer patient at a frequency of at least 10 per 10^4 PBLs.

[2] AK Steel Corp. v. Sollac & Ugine, 344 F.3d 1234, 1244 (Fed. Cir. 2003); see also In re Wands, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988).

preclude enablement; what is required is that the amount of experimentation 'must not be unduly extensive.'"[3]

Applicants note that the claims have been amended to remove the recitation of vaccine or pharmaceutical composition, and now recite an immunogenic composition. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection regarding the recitation or use of the terms vaccine and pharmaceutical composition.

As noted above, the Office Action interprets the claim for examination purposes to include peptides incorporating a subsequence of SEQ ID NO:5 with undisclosed flanking sequences not necessarily from the protein of origin. Following this interpretation presented in the Office Action, Applicants submit that a reasonably representative number of epitope peptides meeting the elements of claim 1 are set forth in the specification. For example, the specification contemplates the epitope peptides Sur9 (SEQ ID NO:3) and Sur1L2 (SEQ ID NO:4), which each comprise a subsequence of SEQ ID NO:5 (namely "LGEFLKL"). *See* specification, page 23, Table 1. Furthermore, all three of these epitope-derived peptides have C_{50} (μM) values of at most 20 μM. *Id.* Accordingly, Applicants submit that a reasonably representative number of epitope-derived peptides is presented in the specification to support the scope of the amended claims.

Furthermore, Applicants reiterate their prior remarks regarding the M.P.E.P. statement that "Office personnel should not impose on applicants the unnecessary burden of providing evidence from human clinical trials ... Thus, as a general rule, if an applicant has initiated human clinical trials for a therapeutic product or process, Office personnel should presume that the applicant has established that the subject matter of that trial is reasonably predictive of having the asserted therapeutic utility."[4]

In other words, the disclosure of clinical data in the instant case is presumptive evidence that *supports* -- not undermines -- enablement of the claimed compositions. Regarding the Reker

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[3] PPG Indus., Inc. v. Guardian Indus., Corp., 75 F.3d 1558, 1564, U.S.P.Q.2d 1618, 1623 (Fed. Cir. 1996) (quoting Atlas Powder Co. v. E.I. DuPont de Nemours & Co., 750 F.2d 1569, 1576 (Fed. Cir. 1984)).

et al reference, Dr. Andersen explained that the "statement was presented in the discussion of the research data, not to express concerns with respect to the relevance of using survivin peptides in cancer immunotherapy, but merely to indicate that phase III clinical trials - the only firm proof that a vaccine works - had not yet been completed."[5]

Also, the M.P.E.P. states that "... data generated using *in vitro* assays, or from testing in an animal model or a combination thereof almost invariably will be sufficient to establish therapeutic or pharmacological utility for a compound, composition or process" so long as the data is reasonably correlated to the asserted utility.[6] Under this standard, "[t]he applicant does not have to prove that a correlation exists between a particular activity and an asserted therapeutic use of a compound as a matter of statistical certainty, nor does he or she have to provide actual evidence of success in treating humans where such a utility is asserted."[7]

The instant application meets this standard because the Examples disclose data from multiple *in vitro* assays that adequately establish therapeutic utility of the claimed peptide compositions—including immunogenic compositions:

Example 1 of the instant application provides data from *in vitro* assays measuring binding of the Sur1M2 peptide (SEQ ID NO:5), the Sur9 peptide (SEQ ID NO:3) and the Sur1L2 peptide (SEQ ID NO:4) to Class I MHC molecules and quantifying its ability to induce a Cytotoxic T-Lymphocyte (CTL) response. The results reveal high-affinity binding of Sur1M2 and Sur1L2 peptides to HLA-A2 (C_{50} = 1 μM) — a level similar to the positive control, and relatively high-affinity binding of the Sur9 peptide to HLA-A2 (C_{50} = 10 μM). *See* specification, pages 23-25.

It is also noted that in Example 2 of the specification the reactivity of three epitope-derived peptides (Sur1, Sur9, Sur1M2) was measured in peripheral blood lymphocytes (PBLs) by ELISPOT from ten HLA-A2 positive breast cancer patients, fourteen HLA-A2 positive melanoma patients, and six chronic lymphatic leukemia (CLL) patients. According to the

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[4] MPEP § 2107.03 (IV)("Human Clinical Data") (8th Ed., 7th Rev.) (emphasis in original).

[5] *See* Declaration under 37 C.F.R. § 1.132 of Dr. Mads Hald Andersen, of record.

[6] M.P.E.P. § 2107.03(III) ("Data From *In Vitro* or Animal Testing ...") (8th Ed., 7th Rev.).

[7] Nelson v. Bowler, 626 F.2d 853, 857, 206 U.S.P.Q. 881, 884 (C.C.P.A. 1980); M.P.E.P. 2107.03(I).

specification, "[t]he ELISPOT assay was used to quantify peptide epitope-specific IFN-γ releasing effector cells and has been described previously ..." *See* specification, page 27, lines 30-31.

The results demonstrate that at least several patients, represented by each category of cancer, responded to each of the respective epitope-derived peptides by eliciting IFN-γ producing cells at a frequency of at least 10 per 10^4 PBL. *See* specification, page 29, Table 2. Thus, Applicants submit that a reasonably representative number of epitope-derived peptides comprising SEQ ID NO:5 (as interpreted in the Office Action) satisfy the elements of dependent claim 21 as well.[8] Applicants submit that these results provide further evidence that compositions based on the Sur1M2, Sur1 and Sur9 epitope peptides have immunogenicity and are able to induce highly specific CTLs capable of killing tumor target cells.

In sum, Applicants submit that the extensive *in vitro* data disclosed in the instant application provides evidence that the Sur1M2 and Sur9 peptides can bind with high-affinity to an MHC Class I molecule and induce a specific and strong CTL response that can infiltrate cancerous tissue. Accordingly, Applicants submit that the scope of claims in the instant application is reasonably commensurate with the scope of the enabling disclosure.[9] In light of the instant amendments and remarks provided herein, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1, 21, 23-25, 33-36, and 38-40 under 35 U.S.C. § 112, 1st paragraph as allegedly failing to comply with the enablement requirement. Applicants note that rejected claims 28 and 50 are cancelled herein without prejudice or disclaimer.

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[8] Claim 21 recites: A peptide according to claim 1 that is capable of eliciting INF-γ -producing cells in a PBL population of a cancer patient at a frequency of at least 10 per 10^4 PBLs.

[9] See In re Wright, 999 F.2d 155, 27 U.S.P.Q.2d 1510 (Fed. Cir. 1993) ("The scope of the claims must bear a reasonable relationship to the scope of enablement.").

- **Claim 24**

Claim 24 was rejected under 35 U.S.C. § 112, 1st paragraph as allegedly failing to comply with the enablement requirement. The Office Action asserts that there is insufficient disclosure in the specification on the breast cancer cell line MCF-7 and melanoma cell line FM3. The Examiner appears to be taking the position that the designations MCF-7 and FM3 are "merely a laboratory designation which does not clearly define the claimed product". *See* Office Action, page 18.

Applicants respectfully disagree and traverse.

Applicants reiterate that the breast cancer cell line MCF-7 is commercially available from the LGC Promochem / ATCC as ATCC Number HTB-22 ™, and thus it is not an undue burden on the skilled artisan to obtain this cell line. (*See* http://www.lgcstandards-atcc.org/LGCAdvancedCatalogueSearch/ProductDescription/tabid/1068/Default.aspx). For the Examiner's convenience, Applicants include herewith as Appendix A the printout from the LGC / ATCC website showing the availability of MCF-7 from LGC / ATCC as ATCC Number HTB-22 ™. Applicants also include herewith as Appendix B a printout from the LGC / ATCC website of the "Commercial Use" provisions for biological materials. It is Applicants' understanding that LGC / ATCC products are available primarily for non-commercial use, but that non-exclusive licenses are available for certain commercial uses including those listed in Appendix B.

Applicants respectfully submit that the designation MCF-7 represents a well-known and publicly available breast cancer cell line. This is reflected for example in issued U.S. Patent No. 4,753,894, issued June 28, 1988, which recites MCF-7 in the issued claims. Applicants note that issued patents carry a presumption of enablement for the claimed subject matter.

This can also be seen from literature references, such as for example the post-filing publication of Lu *et al* (attached herewith as Appendix C). This is even reflected in the free encyclopedia "Wikipedia" which, while not generally considered a peer-reviewed source of publications, nonetheless reflects the general sentiment that MCF-7 is a "common" cell line (attached herewith as Appendix D).

Regarding the melanoma cell line FM3, it is Applicants' understanding that this cell line is available to researchers from the ESTDAB database cell bank at a nominal cost structured to cover the costs incurred by ESTDAB in the preparation of the cell line order.

Applicants respectfully request reconsideration and withdrawal of the rejection of claim 24 under 35 U.S.C. § 112, 1st paragraph.

35 U.S.C. § 112, 2nd paragraph

- **Claim 1**

Claim 1 was rejected as indefinite in the recitation of "epitope peptide". Applicants submit that this rejection has been rendered moot by way of claim amendment, and respectfully request reconsideration and withdrawal of the rejection of claim 1 as indefinite.

- **Claim 24**

Claim 24 was rejected as indefinite in the recitation of "... the breast cancer cell line MCF-7 and the melanoma cell line FM3." Applicants submit that the recitation of breast cancer cell line MCF-7 and melanoma cell line FM3 is not indefinite, as these are art recognized cell lines. For example, the breast cancer cell line MCF-7 is commercially available from the LGC Promochem / ATCC as ATCC Number HTB-22 ™, and thus it is not an undue burden on the skilled artisan to obtain this cell line. (*See* http://www.lgcstandards-atcc.org/LGCAdvancedCatalogueSearch/ProductDescription/tabid/1068/Default.aspx). For the Examiner's convenience, Applicants include herewith as Appendix A the printout from the LGC / ATCC website showing the availability of MCF-7 from LGC / ATCC as ATCC Number HTB-22 ™. Applicants also include herewith as Appendix B a printout from the LGC / ATCC website of the "Commercial Use" provisions for biological materials. It is Applicants' understanding that LGC / ATCC products are available primarily for non-commercial use, but that non-exclusive licenses are available for certain commercial uses including those listed in Appendix B.

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Regarding the melanoma cell line FM3, it is Applicants' understanding that this cell line is available to researchers from the ESTDAB database cell bank at a nominal cost structured to cover the costs incurred by ESTDAB in the preparation of the cell line order.

- **Claims 33 and 35**

Claims 33 and 35 were rejected as indefinite in the recitation of "vaccine" and "vaccinated". Applicants submit that this rejection has been rendered moot by way of claim amendments, and respectfully request reconsideration and withdrawal of the rejection of claims 33 and 35 as indefinite.

Prior Art Rejections

Applicants appreciate the Examiner's reconsideration and withdrawal of the previous prior art rejections, as evidenced on pages 25-26 of the Office Action. Applicants provide the following remarks in reply to the current prior art rejections.

- **Andersen References**

As an initial matter, Applicants respectfully address the characterization of both of the cited Andersen references as prior art. Applicants submit that the earliest priority filing (U.S. provisional patent application no. 60/352,284) was filed on January 30, 2002, and includes disclosure of at least SEQ ID NO:5, to which amended claim 1 is now directed. Claim 1 has also been amended to recite a C_{50} of at most 20, which finds literal support in the priority application

in at least the exemplary support identified in the table below. Furthermore, exemplary support for each of the remaining claims may be found in at least the following text of the priority filing:

Current Claim	Exemplary Support in Priority Filing
1	p. 3, Table 1 and lines 19-20; p. 5, lines 2-11; p. 23, lines 4-9.
21	p. 4, lines 5-15; p. 5, lines 12-26; and Figure 2
23	p. 2, lines 18-19; p. 7, lines 26-29; p. 9, lines 9-14 and 23-31; and p. 14, lines 29-39
24	p. 10, line 39 extending to p. 11, line 2; p. 11, lines 40 extending to p. 12, line 12
25	p. 23, line 42 extending to page 24, line 1.
33	p. 3, Table 1; p. 11, lines 5-18; and p.12, lines 15-35
34	p. 2, lines 18-19; p. 7, lines 26-29; p. 9, lines 9-14 and 23-31; and p. 14, lines 29-39
35	p. 3, Table 1; p. 11, lines 5-18; and p.12, lines 15-35
36	p. 23, lines 35-41
38	p. 23, lines 31-33
39	p. 23, lines 31-33
40	p. 23, lines 31-33

As discussed above, Applicants note that the Office Action interprets the recitation of a MHC Class I-restricted epitope composition comprising the epitope peptide of SEQ ID NO:5 as

including a subsequence of SEQ ID NO:5. *See* Office Action, page 3, lines 8-10. Following this interpretation, Applicants submit that an adequate representative number of MHC Class I-restricted epitope peptides satisfying the recited C_{50} value of at most 20 are disclosed. For example, Sur9 and Sur1L2 each comprise a subsequence of SEQ ID NO:5 (namely "LGEFLKL"), and have C_{50} values of at most 20. *See* page 3, table of the priority application. Therefore, Applicants submit that the full scope of claim 1 is adequately supported in the provisional application.

Applicants appreciate the Examiner's acknowledgement of the publishing error regarding the Anderson reference published in volume 61, publication date 2/2001. The remaining question appears to be adequate support for the claims in the afore-mentioned provisional priority application. For the reasons set forth above, Applicants submit that the amended claims find proper support in the priority application as originally filed, and respectfully request consideration and confirmation of this support for the amended claims. Because Applicants' provisional application was filed less than one year after the publication of the two Andersen references, and because the amended claims find proper support in the provisional application as originally filed, Applicants submit that the Andersen references are not prior art under 35 U.S.C. § 102(b).

Furthermore, Applicants reiterate that they have previously submitted a declaration under 37 C.F.R. § 1.132 by inventor Mads Hald Andersen (of record), in which Dr. Andersen sets forth the contribution of each of the non-inventor and inventor authors of the two cited Andersen publications. Applicants submit that the declaration of Dr. Andersen establishes that the cited Andersen *et al* articles are describing Applicants' own work.

- ***35 U.S.C. § 102 (b)***

a) Claims 1, 21, 23, 24, 36 and 38-40 were rejected under 35 U.S.C. § 102 (b), as allegedly anticipated by the disclosure of Andersen *et al* (Cancer Res., 2/2001, 61:869-872) as evidenced by Andersen *et al* (Cancer Res., 2001, 61:5964-5968).

Applicants respectfully disagree and traverse this rejection.

As discussed above, Applicants believe that neither of the cited Andersen *et al* references is prior art under 35 U.S.C. § 102 (b) to the claimed invention for the reasons provided. The amended claims find full support in the provisional application as originally filed. Furthermore, Applicants submit that the declaration of Dr. Andersen under 37 C.F.R. § 1.132 establishes that the Andersen *et al* articles are describing Applicants' own work. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1, 21, 23, 24, 36 and 38-40 under 35 U.S.C. § 102 (b).

b) Claims 1, 21, 23, 24, 36 and 38-40 were rejected under 35 U.S.C. § 102 (b), as allegedly anticipated by the disclosure of Andersen *et al* (Cancer Res., 2001, 61:5964-5968).

Applicants respectfully disagree and traverse this rejection.

As discussed above, Applicants believe that neither of the cited Andersen *et al* references is prior art under 35 U.S.C. § 102 (b) to the claimed invention for the reasons provided. The amended claims find full support in the provisional application as originally filed. Furthermore, Applicants submit that the declaration of Dr. Andersen under 37 C.F.R. § 1.132 establishes that the Andersen *et al* articles are describing Applicants' own work. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1, 21, 23, 24, 36 and 38-40 under 35 U.S.C. § 102 (b).

c) Claims 1, 21, 23-25, 28, 33-35, 36, 38-40, and 50 were rejected under 35 U.S.C. § 102 (b), as allegedly anticipated by the disclosure of International Publication No. WO 02/072631 (9/19/2002).

Applicants respectfully disagree and traverse this rejection.

As an initial matter, it is noted that International Publication No. WO 02/072631 (9/19/2002) recites the designation coined by the instant inventor and corresponding to SEQ ID NO:5, namely "Sur1M2", therefore suggesting that the authors of International Publication No. WO 02/072631 (9/19/2002) were aware the inventors published work.

Substantively, Applicants believe that International Publication No. WO 02/072631 is not prior art under 35 U.S.C. § 102 (b) to the claimed invention for the reasons provided. The amended claims find full support in the provisional application as originally filed, and therefore are accorded the benefit of priority to January 30, 2002. International Publication No. WO 02/072631 published on September 19, 2002, and therefore is unavailable as prior art under 35 U.S.C. § 102(b). Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1, 21, 23, 24, 36 and 38-40 under 35 U.S.C. § 102 (b).

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1, 21, 23-25, 28, 33-35, 36, 38-40, and 50 under 35 U.S.C. § 102 (b).

- ***35 U.S.C. § 103(a)***

a) Claims 1, 21, 23-25, 28, 33-36, 38-40, and 50 were rejected under 35 U.S.C. § 103(a) as allegedly obvious over Anderson et al (2001, 61:5964-5968) in view of U.S. Patent No. 6,572,864.

Applicants respectfully disagree and traverse this rejection.

As discussed above, Applicants believe that neither of the cited Andersen *et al* references is prior art under 35 U.S.C. § 102 (b) to the claimed invention for the reasons provided, and therefore is also not available as prior art under 35 U.S.C. § 103. See M.P.E.P. § 2141.01. The amended claims find full support in the provisional application as originally filed. Furthermore, Applicants submit that the declaration of Dr. Andersen under 37 C.F.R. § 1.132 establishes that the Andersen *et al* articles are describing Applicants' own work. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1, 21, 23-25, 28, 33-36, 38-40, and 50 under 35 U.S.C. § 103(a).

b) Claims 1, 21, 23-25, 28, 33-36, 38-40, and 50 were rejected under 35 U.S.C. § 103(a) as allegedly obvious over Anderson et al (2/2001, 61:869-872) in view of U.S. Patent No. 6,572,864.

Applicants respectfully disagree and traverse this rejection.

As discussed above, Applicants believe that neither of the cited Andersen *et al* references is prior art under 35 U.S.C. § 102 (b) to the claimed invention for the reasons provided, and therefore is also not available as prior art under 35 U.S.C. § 103. See M.P.E.P. § 2141.01. The amended claims find full support in the provisional application as originally filed. Furthermore, Applicants submit that the declaration of Dr. Andersen under 37 C.F.R. § 1.132 establishes that the Andersen *et al* articles are describing Applicants' own work. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1, 21, 23-25, 28, 33-36, 38-40, and 50 under 35 U.S.C. § 103(a).

- ***Obviousness-Type Double Patenting***

a) Claims 1, 21, 23-25, 28, 33-36, 38-40 and 50 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting over claims 1, 4-7, 14, 17-24, 26-34, and 44 of co-pending Application No. 10/354,090, in view of Anderson *et al* (Cancer Res. 2/2001, 61:869-872) or International Publication No. WO 02/072631. Applicants submit herewith a Terminal Disclaimer, thereby obviating this rejection. Applicants respectfully request reconsideration and withdrawal of this nonstatutory obviousness-type double patenting rejection over co-pending Application No. 10/354,090 in view of Anderson *et al* or International Publication No. WO 02/072631.

b) Claims 1, 21, 23-25, 28, 33-36, and 50 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting over claims 1-3, 6, 9, 11, 12, 14-16, 27-37, and 44 of co-pending Application No. 10/543,755. Applicants submit herewith a Terminal Disclaimer, thereby obviating this rejection. Applicants respectfully request reconsideration and withdrawal of this nonstatutory obviousness-type double patenting rejection over co-pending Application No. 10/543,755.

c) Claims 38-40 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting over claims 1-3, 6, 9, 11, 12, 14-16, 27-37, and 44 of co-pending

Application No. 10/543,755, in view of International Publication No. WO 02/072631. Applicants submit herewith a Terminal Disclaimer, thereby obviating this rejection. Applicants respectfully request reconsideration and withdrawal of this nonstatutory obviousness-type double patenting rejection over co-pending Application No. 10/543,755 in view of International Publication No. WO 02/072631.

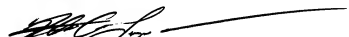
CONCLUSION

An indication of allowance of all claims is respectfully solicited. Early notification of a favorable consideration is respectfully requested.

Respectfully submitted,

HUNTON & WILLIAMS LLP

Date: August 17, 2009

By: 
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